Access DB# 95389

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Hong Liu Examiner #: 77011 Date: 5/29/03
Art Unit: 1624 Phone Number 30 6-5814 Serial Number: 09/688,756
Mail Box and Bldg/Room Location: 4E01 Results Format Preferred (circle): PAPER DISK E-MAIL
4En MEJ
If mor than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Therapeutic compounds

Inventors (please provide full names): F. Uckun E Sudbeck M Cetkovic

Earliest Priority Filing Date:

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Barb please

treating a UVB-induced inflammatory response by administrating a JAK-3 inhibitor.

RECEIVED MAY 30 2003 (STIC)

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: BOB	NA Sequence (#)		STN	351
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	4	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed: 6-10-03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 20	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 53	Other		Other (specify)	

PTO-1590 (8-01)

STIC Search Report
Biotech-Chem Library

Scientific & Technical Information Center
USPTO

STIC Database Tracking Number: 95389

TO: Hong Liu
Location: cm1/4e01/4e12
Art Unit: 1624
Tuesday, June 10, 2003

Case Serial Number: 688756

From: Barb O'Bryen
Location: Biotech-Chem Library
CM1-6A05
Phone: 308-4291

barbara.obryen@uspto.gov

BOB

Search Notes

sira
Search and Information Resources Administration

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact:***

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

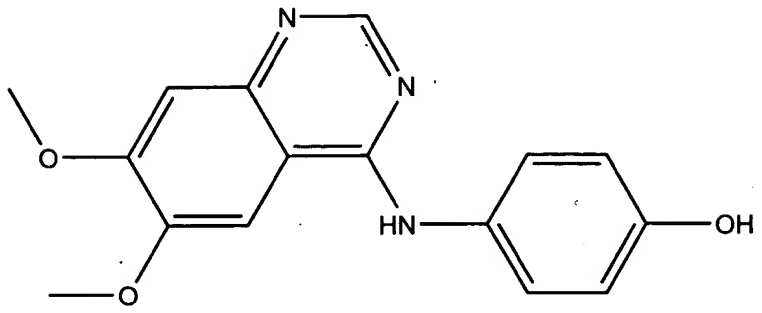
Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

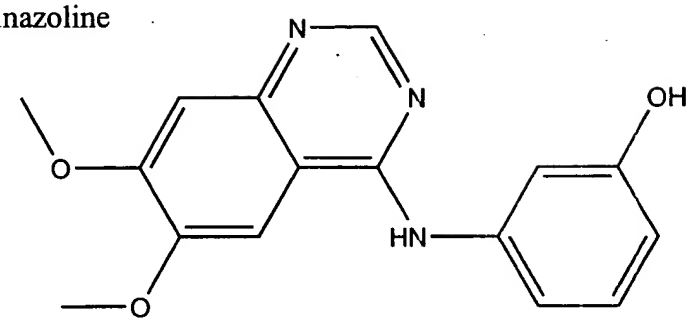
- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

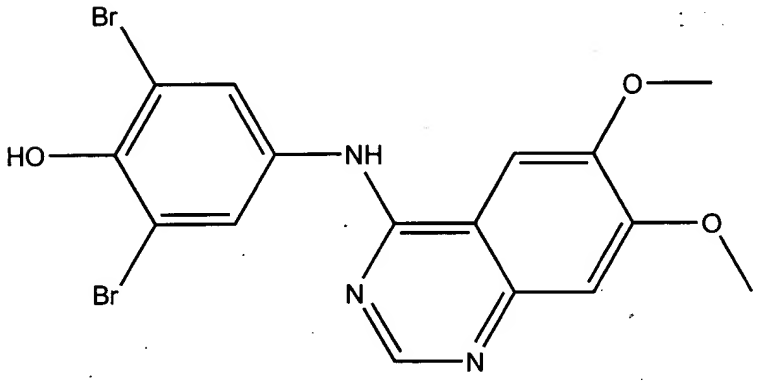
Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk



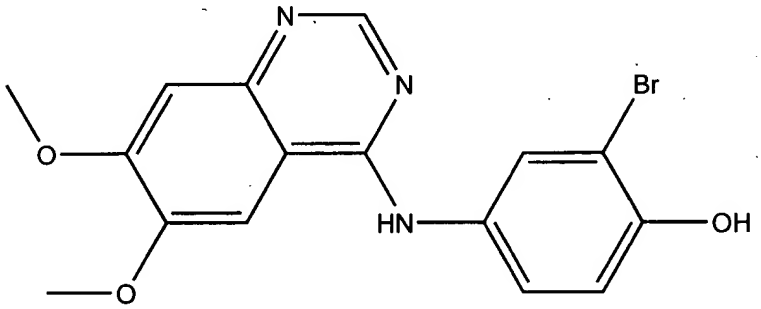
4-(4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline



4-(3'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline



4-(3',5'-dibromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline



4-(3'-bromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline

```
=> fil reg; d ide
FILE 'REGISTRY' ENTERED AT 14:28:19 ON 10 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:     9 JUN 2003  HIGHEST RN 528266-88-8
DICTIONARY FILE UPDATES:    9 JUN 2003  HIGHEST RN 528266-88-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   157482-36-5  REGISTRY
CN   Kinase (phosphorylating), JAK3 protein (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Jak-3 Janus kinase
CN   Jak3 kinase
CN   JAK3 protein (tyrosine) kinase
CN   JAK3 protein kinase
CN   JAK3 tyrosine kinase
CN   Janus kinase 3
CN   L-JAK kinase
CN   Leukocyte Janus kinase
CN   Protein kinase Jak3
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   ADISNEWS, BIOSIS, CA, CAPLUS, CIN, TOXCENTER, USPAT2,
       USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             367 REFERENCES IN FILE CA (1957 TO DATE)
               4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             368 REFERENCES IN FILE CAPLUS (1957 TO DATE)
```
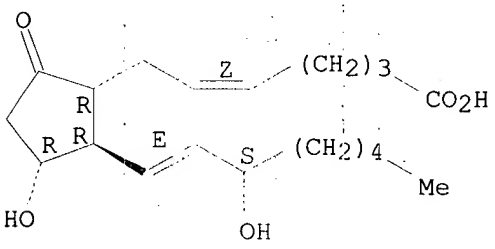

=> d ide

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 363-24-6 REGISTRY
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]- (8CI)
CN 5-Heptenoic acid, 7-[3.alpha.-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]- (7CI)
OTHER NAMES:
CN (-)-Prostaglandin E2
CN (15S)-Prostaglandin E2
CN 11.alpha.,15.alpha.-Dihydroxy-9-ketoprosta-5,13-dienoic acid
CN 11.alpha.,15.alpha.-Dihydroxy-9-oxo-5-cis,13-trans-prostadienoic acid
CN Cervidil
CN Cerviprost
CN Dinoprostone
CN Enzaprost E
CN Glandin
CN l-PGE2
CN l-Prostaglandin E2
CN Minprositin E2
CN Minprostin E2
CN PGE2
CN Prepidil
CN Propess
CN **Prostaglandin E2**
CN Prostarmon E
CN Prostenon
CN Prostenone
CN Prostin
CN Prostin (prostaglandin)
CN Prostin E2
CN U 12062
FS STEREOSEARCH
MF C20 H32 O5
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

23328 REFERENCES IN FILE CA (1957 TO DATE)
115 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
23355 REFERENCES IN FILE CAPLUS (1957 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil reg; d stat que l10
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DICTIONARY FILE UPDATES:    9 JUN 2003  HIGHEST RN 528266-88-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L8                  STR
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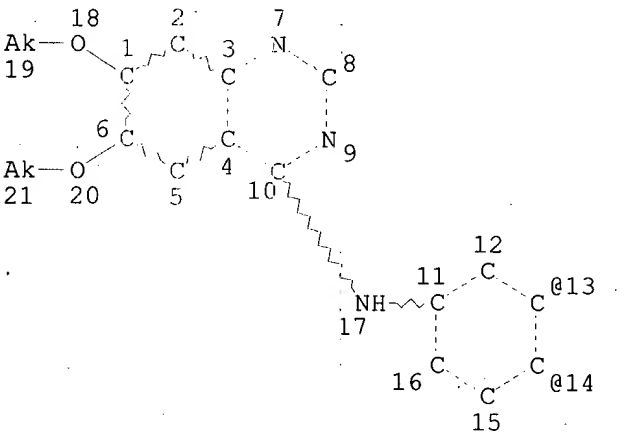

this structure covers the 4 species in the claims

```
VPA 22-13/14 U
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC  11
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L10           72 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED   3581 ITERATIONS                 72 ANSWERS
SEARCH TIME: 00.00.01
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```
=> fil capl; d que nos l22; d que nos l24

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FILE COVERS 1907 - 10 Jun 2003  VOL 138 ISS 24
FILE LAST UPDATED: 9 Jun 2003  (20030609/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L5             1 SEA FILE=REGISTRY ABB=ON  157482-36-5
L8               STR
L10           72 SEA FILE=REGISTRY SSS FUL L8
L11         3589 SEA FILE=CAPLUS ABB=ON  UV B RADIATION+OLD,NT/CT
L12           64 SEA FILE=CAPLUS ABB=ON  L5(L)(INHIBIT? OR ANTAGONI?)/OBI
L13           52 SEA FILE=CAPLUS ABB=ON  L10
L15            1 SEA FILE=REGISTRY ABB=ON  "PROSTAGLANDIN E2"/CN
L16        23366 SEA FILE=CAPLUS ABB=ON  L15
L17         3224 SEA FILE=CAPLUS ABB=ON  (L16 OR "PROSTAGLANDIN E2")(L)(INHIBIT?
                 OR ANTAGONI?)/OBI
L18          377 SEA FILE=CAPLUS ABB=ON  SUNBURN/CT
L19         6774 SEA FILE=CAPLUS ABB=ON  SKIN, NEOPLASM/CT
L20        11992 SEA FILE=CAPLUS ABB=ON  SKIN, DISEASE/CT
L21        26724 SEA FILE=CAPLUS ABB=ON  INFLAMMATION/CT
L22            3 SEA FILE=CAPLUS ABB=ON  (L11 OR (L17 OR L18 OR L19 OR L20 OR
                 L21)) AND (L12 OR L13)


L5             1 SEA FILE=REGISTRY ABB=ON  157482-36-5
L8               STR
L10           72 SEA FILE=REGISTRY SSS FUL L8
L12           64 SEA FILE=CAPLUS ABB=ON  L5(L)(INHIBIT? OR ANTAGONI?)/OBI
L13           52 SEA FILE=CAPLUS ABB=ON  L10
L23         5188 SEA FILE=CAPLUS ABB=ON  UVB OR (UV OR ULTRAVIOLET)(1A)(RAY# OR
                 RADIATION)(1A)B
L24            1 SEA FILE=CAPLUS ABB=ON  L23 AND (L12 OR L13)

=> s l22 or l24

L78            3 L22 OR L24

=> fil medl; d que nos l35; d que nos l36; d que nos l39

FILE 'MEDLINE' ENTERED AT 15:29:40 ON 10 JUN 2003
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FILE LAST UPDATED: 8 JUN 2003 (20030608/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L8              STR
L10              72 SEA FILE=REGISTRY SSS FUL L8
L35               0 SEA FILE=MEDLINE ABB=ON  L10


L25             536 SEA FILE=MEDLINE ABB=ON  (JANUS KINASE OR JAK)(W)3 OR JAK3
L26            3581 SEA FILE=MEDLINE ABB=ON  PROTEIN-TYROSINE KINASE/CT(L)AI/CT
L27           51718 SEA FILE=MEDLINE ABB=ON  ENZYME INHIBITORS/CT
L28              71 SEA FILE=MEDLINE ABB=ON  L25 AND (L26 OR L27)
L29           39211 SEA FILE=MEDLINE ABB=ON  ULTRAVIOLET RAYS/CT
L31           16379 SEA FILE=MEDLINE ABB=ON  DINOPROSTONE/CT
L32            1265 SEA FILE=MEDLINE ABB=ON  SUNBURN/CT
L33           32601 SEA FILE=MEDLINE ABB=ON  INFLAMMATION/CT
L34           13811 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS/CT
L36               0 SEA FILE=MEDLINE ABB=ON  L28 AND (L29 OR (L31 OR L32 OR L33 OR
                    L34))


L25             536 SEA FILE=MEDLINE ABB=ON  (JANUS KINASE OR JAK)(W)3 OR JAK3
L26            3581 SEA FILE=MEDLINE ABB=ON  PROTEIN-TYROSINE KINASE/CT(L)AI/CT
L27           51718 SEA FILE=MEDLINE ABB=ON  ENZYME INHIBITORS/CT
L28              71 SEA FILE=MEDLINE ABB=ON  L25 AND (L26 OR L27)
L37          120073 SEA FILE=MEDLINE ABB=ON  SKIN+NT/CT
L38          401529 SEA FILE=MEDLINE ABB=ON  SKIN DISEASES+NT/CT
L39               2 SEA FILE=MEDLINE ABB=ON  L28 AND (L37 OR L38)
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=> fil embase; d que nos 149; d que nos 151; d que nos 153; d que nos 154; d que nos 156

FILE 'EMBASE' ENTERED AT 15:29:41 ON 10 JUN 2003

FILE COVERS 1974 TO 5 Jun 2003 (20030605/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L8              STR
L10              72 SEA FILE=REGISTRY SSS FUL L8
L40               8 SEA FILE=EMBASE ABB=ON  L10
L41           20864 SEA FILE=EMBASE ABB=ON  ULTRAVIOLET RADIATION/CT
L42            3690 SEA FILE=EMBASE ABB=ON  ULTRAVIOLET B RADIATION/CT
L43             919 SEA FILE=EMBASE ABB=ON  JANUS KINASE/CT
L44              21 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3/CT
L45               3 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3 INHIBITOR/CT
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```
L46           6 SEA FILE=EMBASE ABB=ON  JANUS KINASE INHIBITOR/CT
L47       12887 SEA FILE=EMBASE ABB=ON  ENZYME INHIBITOR/CT
L49           1 SEA FILE=EMBASE ABB=ON  (L41 OR L42) AND (L40 OR (L45 OR L46)
                OR ((L43 OR L44) AND L47))


L8              STR
L10            72 SEA FILE=REGISTRY SSS FUL L8
L40             8 SEA FILE=EMBASE ABB=ON  L10
L43           919 SEA FILE=EMBASE ABB=ON  JANUS KINASE/CT
L44            21 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3/CT
L45             3 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3 INHIBITOR/CT
L46             6 SEA FILE=EMBASE ABB=ON  JANUS KINASE INHIBITOR/CT
L47         12887 SEA FILE=EMBASE ABB=ON  ENZYME INHIBITOR/CT
L50         36878 SEA FILE=EMBASE ABB=ON  SKIN CANCER+NT/CT
L51             2 SEA FILE=EMBASE ABB=ON  L50 AND (L40 OR (L45 OR L46) OR ((L43
                OR L44) AND L47))


L8              STR
L10            72 SEA FILE=REGISTRY SSS FUL L8
L40             8 SEA FILE=EMBASE ABB=ON  L10
L43           919 SEA FILE=EMBASE ABB=ON  JANUS KINASE/CT
L44            21 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3/CT
L45             3 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3 INHIBITOR/CT
L46             6 SEA FILE=EMBASE ABB=ON  JANUS KINASE INHIBITOR/CT
L47         12887 SEA FILE=EMBASE ABB=ON  ENZYME INHIBITOR/CT
L52        692334 SEA FILE=EMBASE ABB=ON  INFLAMMATION+NT/CT
L53             1 SEA FILE=EMBASE ABB=ON  L52 AND (L40 OR (L45 OR L46) OR ((L43
                OR L44) AND L47))


L8              STR
L10            72 SEA FILE=REGISTRY SSS FUL L8
L40             8 SEA FILE=EMBASE ABB=ON  L10
L43           919 SEA FILE=EMBASE ABB=ON  JANUS KINASE/CT
L44            21 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3/CT
L45             3 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3 INHIBITOR/CT
L46             6 SEA FILE=EMBASE ABB=ON  JANUS KINASE INHIBITOR/CT
L47         12887 SEA FILE=EMBASE ABB=ON  ENZYME INHIBITOR/CT
L48         25557 SEA FILE=EMBASE ABB=ON  "PROSTAGLANDIN E2"/CT
L54             1 SEA FILE=EMBASE ABB=ON  L48 AND (L40 OR (L45 OR L46) OR ((L43
                OR L44) AND L47))


L8              STR
L10            72 SEA FILE=REGISTRY SSS FUL L8
L40             8 SEA FILE=EMBASE ABB=ON  L10
L43           919 SEA FILE=EMBASE ABB=ON  JANUS KINASE/CT
L44            21 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3/CT
L45             3 SEA FILE=EMBASE ABB=ON  JANUS KINASE 3 INHIBITOR/CT
L46             6 SEA FILE=EMBASE ABB=ON  JANUS KINASE INHIBITOR/CT
L47         12887 SEA FILE=EMBASE ABB=ON  ENZYME INHIBITOR/CT
L55          1040 SEA FILE=EMBASE ABB=ON  SUNBURN/CT
L56             0 SEA FILE=EMBASE ABB=ON  L55 AND (L40 OR (L45 OR L46) OR ((L43
                OR L44) AND L47))

=> s 149 or 151 or 153 or 154
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```
L79          3 L49 OR L51 OR L53 OR L54

=> fil uspatf; d que nos 162; d que nos 164;s 162 or 164

FILE 'USPATFULL' ENTERED AT 15:29:42 ON 10 JUN 2003
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Jun 2003 (20030610/PD)
FILE LAST UPDATED: 10 Jun 2003 (20030610/ED)
HIGHEST GRANTED PATENT NUMBER: US6578203
HIGHEST APPLICATION PUBLICATION NUMBER: US2003106125
CA INDEXING IS CURRENT THROUGH 10 Jun 2003 (20030610/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Jun 2003 (20030610/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

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L5             1 SEA FILE=REGISTRY ABB=ON  157482-36-5
L8               STR
L10           72 SEA FILE=REGISTRY SSS FUL L8
L57           35 SEA FILE=USPATFULL ABB=ON  L10
L58           40 SEA FILE=USPATFULL ABB=ON  (JAK3 OR (JANUS KINASE OR JAK)(W)3)/
                 IT,TI,AB,CLM OR L5
L59           15 SEA FILE=USPATFULL ABB=ON  L58(3A)(INHIBIT?)/IT,TI,AB,CLM
L60         2457 SEA FILE=USPATFULL ABB=ON  (SUNBURN OR SKIN(3A)(CANCER? OR
                 NEOPLAS? OR CARCINOMA?) OR UVB OR (ULTRAVIOLET OR UV)(W)B)/IT,T
                 I,AB,CLM
L61          190 SEA FILE=USPATFULL ABB=ON  "PROSTAGLANDIN E2"/IT,TI,AB,CLM
L62            3 SEA FILE=USPATFULL ABB=ON  (L57 OR L59) AND (L60 OR L61)



L5             1 SEA FILE=REGISTRY ABB=ON  157482-36-5
L8               STR
L10           72 SEA FILE=REGISTRY SSS FUL L8
L57           35 SEA FILE=USPATFULL ABB=ON  L10
L58           40 SEA FILE=USPATFULL ABB=ON  (JAK3 OR (JANUS KINASE OR JAK)(W)3)/
                 IT,TI,AB,CLM OR L5
L59           15 SEA FILE=USPATFULL ABB=ON  L58(3A)(INHIBIT?)/IT,TI,AB,CLM
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L63       21013 SEA FILE=USPATFULL ABB=ON  INFLAMM?/IT,TI,AB,CLM OR ANTIINFLAM?
                /IT,TI,AB,CLM
L64           5 SEA FILE=USPATFULL ABB=ON  L63 AND (L57 OR L59)


L80           5 L62 OR L64

=> fil CANCERLIT, VETU, DRUGU, BIOTECHNO, CABA, IPA, BIOSIS, TOXCENTER

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FILE 'TOXCENTER' ENTERED AT 15:29:43 ON 10 JUN 2003
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=> d que nos l75

L8              STR
L10            72 SEA FILE=REGISTRY SSS FUL L8
L65            58 SEA L10
L66         97196 SEA (SUNBURN OR SKIN(3A)(CANCER? OR NEOPLAS? OR CARCINOMA?) OR
                UVB OR (ULTRAVIOLET OR UV)(W) B)
L67        633573 SEA INFLAMM? OR ANTIINFLAMM?
L68           179 SEA (JAK3 OR (JANUS KINASE OR JAK)(W) 3)(3A) INHIBIT?
L75            13 SEA (L65 OR L68) AND (L66 OR L67)


=> dup rem l78,l80,l39,l79,l75
FILE 'CAPLUS' ENTERED AT 15:30:11 ON 10 JUN 2003
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FILE 'BIOTECHNO' ENTERED AT 15:30:11 ON 10 JUN 2003
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FILE 'BIOSIS' ENTERED AT 15:30:11 ON 10 JUN 2003

FILE 'TOXCENTER' ENTERED AT 15:30:11 ON 10 JUN 2003

PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L79
PROCESSING COMPLETED FOR L75
L81 19 DUP REM L78 L80 L39 L79 L75 (7 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS
ANSWERS '4-8' FROM FILE USPATFULL
ANSWER '9' FROM FILE MEDLINE
ANSWERS '10-12' FROM FILE EMBASE
ANSWERS '13-15' FROM FILE DRUGU
ANSWERS '16-17' FROM FILE BIOTECHNO
ANSWERS '18-19' FROM FILE BIOSIS

=> d ibib abs hitstr 1-8;d iall 9-19

L81 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2000:144864 CAPLUS
DOCUMENT NUMBER: 132:189690
TITLE: Therapeutic uses of quinazoline derivatives as JAK-3 kinase inhibitors
INVENTOR(S): Navara, Christopher S.; Mahajan, Sandeep; Uckun, Fatih M.
PATENT ASSIGNEE(S): Hughes Institute, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010981	A1	20000302	WO 1999-US19043	19990820
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2342503	AA	20000302	CA 1999-2342503	19990820
AU 9956827	A1	20000314	AU 1999-56827	19990820
EP 1105378	A1	20010613	EP 1999-943800	19990820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6313129	B1	20011106	US 1999-378093	19990820
JP 2002523403	T2	20020730	JP 2000-566255	19990820
NO 2001000887	A	20010423	NO 2001-887	20010221
US 2001044442	A1	20011122	US 2001-812098	20010319
US 6495556	B2	20021217		
US 2002042513	A1	20020411	US 2001-858824	20010516
US 6469013	B2	20021022		

PRIORITY APPLN. INFO.: US 1998-97359P P 19980821

US 1998-97365P P 19980821
US 1999-378093 A1 19990820
WO 1999-US19043 W 19990820
US 2000-688756 A3 20001016

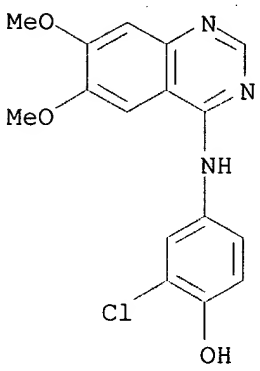
OTHER SOURCE(S): MARPAT 132:189690

AB The invention provides novel JAK-3 kinase inhibitors that are useful for treating leukemia and lymphoma. The compds. are also useful to treat or prevent skin cancer, as well as sunburn and **UVB**-induced skin inflammation. In addn., the compds. of the present invention prevent the immunosuppressive effects of **UVB** radiation, and are useful to treat or prevent autoimmune diseases, inflammation, and transplant rejection. The invention also provides pharmaceutical compns. comprising compds. of the invention, as well as therapeutic methods for their use. For example, treatments with 50 mg/kg or 75 mg/kg of a quinazoline deriv. WHI-P131 (prepn. given) were as effective as cyclosporin A treatment in prolongation of islet allograft survival in mice.

IT **211555-09-8P**, WHI-P 197
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 197; therapeutic uses of quinazoline derivs. as JAK-3 kinase inhibitors)

RN 211555-09-8 CAPLUS

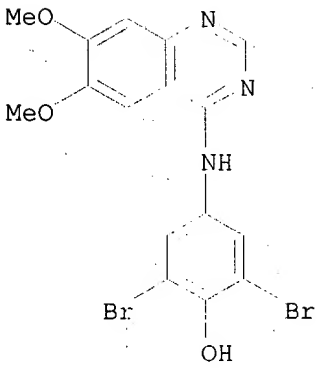
CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **211555-05-4P**, WHI-P 97
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 97; therapeutic uses of quinazoline derivs. as JAK-3 kinase inhibitors)

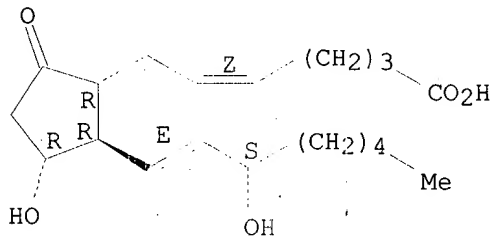
RN 211555-05-4 CAPLUS

CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

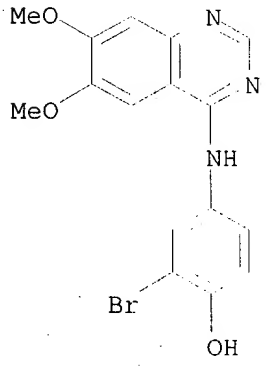


IT **363-24-6, Prostaglandin E2**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**inhibition** of release of; therapeutic uses of quinazoline derivs. as JAK-3 kinase **inhibitors**)
RN 363-24-6 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

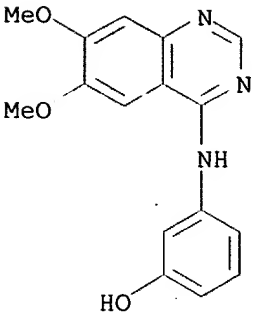
Absolute stereochemistry.
Double bond geometry as shown.



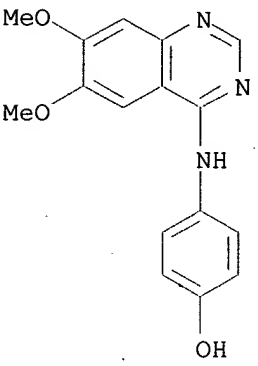
IT **211555-04-3P**, WHI-P154 **211555-08-7P**, WHI-P180
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic uses of quinazoline derivs. as JAK-3 kinase inhibitors)
RN 211555-04-3 CAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-08-7 CAPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **202475-60-3P**, WHI-P131
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic uses of quinazoline derivs. as JAK-3 kinase inhibitors)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5**, Jak3 kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of quinazoline derivs. as JAK-3 kinase **inhibitors**)
RN 157482-36-5 CAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 1997:419875 CAPLUS
DOCUMENT NUMBER: 127:147697
TITLE: Constitutive activation of a slowly migrating isoform of Stat3 in mycosis fungoides: tyrphostin AG490 inhibits Stat3 activation and growth of mycosis fungoides tumor cell lines
AUTHOR(S): Nielsen, Mette; Kaltoft, Keld; Nordahl, Mette; Ropke, Carsten; Geisler, Carsten; Mustelin, Tomas; Dobson,

Pauline; Svejgaard, Arne; Oedum, Niels
CORPORATE SOURCE: Institutes of Medical Microbiology and Immunology, University of Copenhagen, Copenhagen, 2200 N, Den.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(13), 6764-6769
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mycosis fungoides (MF) is a low-grade cutaneous T cell lymphoma of unknown etiol. In this report, the Jak/Stat (Janus kinase/signal transducer and activator of transcription) signaling pathway was investigated in tumor cell lines established from skin biopsy specimens from a patient with MF. Jaks link cytokine receptors to Stats, and abnormal Jak/Stat signaling has been obsd. in some hemopoietic cancers. In MF tumor cells, a slowly migrating isoform of Stat3, Stat3sm, was constitutively activated, i.e., (i) Stat3sm was constitutively phosphorylated on tyrosine residues, and tyrosine phosphorylation was not enhanced by growth factor stimulation; (ii) band shift assays and immunopptns. of DNA/Stat complexes showed constitutive DNA-binding properties of Stat3sm; and (iii) Stat3sm was constitutively assocd. with Jak3. The abnormal activation of Stat3sm was highly specific. Thus, neither the fast migrating isoform of Stat3 (Stat3fm) nor other Stats (Stat1, Stat2, and Stat4 through Stat6) were constitutively activated. The Jak kinase inhibitor, tyrphostin AG490, blocked the constitutive activation of Stat3sm and inhibited spontaneous as well as interleukin 2-induced growth of MF tumor cells. In conclusion, the authors have provided evidence for an abnormal Jak/Stat signaling and growth regulation in tumor cells obtained from affected skin of an MF patient.

IT **157482-36-5**, JAK3 protein kinase
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Stat3sm assocn. with; constitutive activation of slowly migrating isoform of Stat3 in human mycosis fungoides and **inhibition** by tyrphostin AG490 which also **inhibits** growth of mycosis fungoides tumor cell lines)

RN 157482-36-5 CAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L81 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:857390 CAPLUS
DOCUMENT NUMBER: 138:54231
TITLE: Altered biological activity associated with C-terminal modifications of IL-7
AUTHOR(S): Goerguen, Guellue; van der Spek, Johanna; Cosenza, Larry; Menevse, Adnan; Foss, Francine
CORPORATE SOURCE: Tufts New England Medical Center, Boston, MA, 02111, USA
SOURCE: Cytokine+ (2002), 20(1), 17-22
CODEN: CYTIE9; ISSN: 1043-4666
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interleukin 7 (IL-7) is a pleiotropic cytokine which plays a role in both T and B cell function as well as in establishment and maintenance of immunol. barriers in epithelial tissues. The heterodimeric IL-7 receptor (IL-7R) consists of the p76 IL-7R.alpha. subunit and the p64 common gamma (.gamma.c) subunit. Ligand-binding induces signal transduction through tyrosine phosphorylation of the janus (Jak) and src-related kinases as well as by activation of phosphatidylinositol-3 kinase (P13-kinase). In

an effort to further define the requirements for ligand-receptor interactions and to subsequently develop candidate receptor binding antagonists with selective biol. activities, the authors examd. a series of IL-7 mutants in which the C-terminal hydrophobic residues were substituted with aliph. amino acids. In this study the authors describe abrogation of IL-7 driven proliferation and attenuated phosphotyrosine signaling by IL-7(143) (Trp-Ala) and IL-7(143) (Trp-His) in IL-7R expressing T and B leukemia cells. Decreased phosphorylation of Jak3 kinase by IL-7W143A, IL-7W143P and IL-7W143H suggest that alterations in this region of the C-terminal region of IL-7 affects its interaction with the .gamma.c subunit of the IL-7R.

IT **157482-36-5**, JAK3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (receptor-induced activation is **inhibited** by interleukin-7 **antagonists**)
RN 157482-36-5 CAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 4 OF 19 USPATFULL DUPLICATE 2
ACCESSION NUMBER: 2001:197026 USPATFULL
TITLE: Therapeutic compounds
INVENTOR(S): Uckun, Fatih M., White Bear Lake, MN, United States
Sudbeck, Elise A., St. Paul, MN, United States
Cetkovic, Marina, Maplewood, MN, United States
Malaviya, Ravi, Shoreview, MN, United States
Liu, Xing-Ping, Minneapolis, MN, United States
PATENT ASSIGNEE(S): Hughes Institute, St, Paul, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6313129	B1	20011106	
APPLICATION INFO.:	US 1999-378093		19990820	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-97365P	19980821 (60)

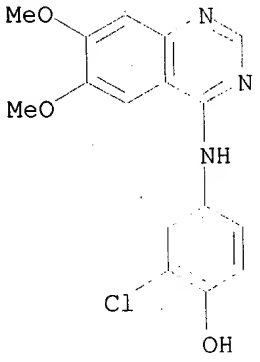
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ford, John M.
ASSISTANT EXAMINER: Liu, Hong
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 42 Drawing Figure(s); 55 Drawing Page(s)
LINE COUNT: 2707
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides novel **JAK-3 inhibitors** that are useful for treating leukemia and lymphoma. The compounds are also useful to treat or prevent **skin cancer**, as well as **sunburn** and **UVB**-induced skin **inflammation**. In addition, the compounds of the present invention prevent the immunosuppressive effects of **UVB** radiation, and are useful to treat or prevent autoimmune diseases, **inflammation**, and transplant rejection. The invention also provides pharmaceutical compositions comprising compounds of the invention, as well as therapeutic methods for their use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **211555-09-8P**, WHI-P 197

(WHI-P 197; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

RN 211555-09-8 USPATFULL

CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

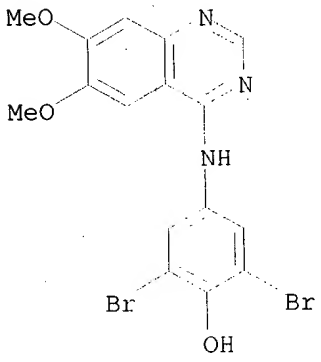


IT **211555-05-4P**, WHI-P 97

(WHI-P 97; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

RN 211555-05-4 USPATFULL

CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

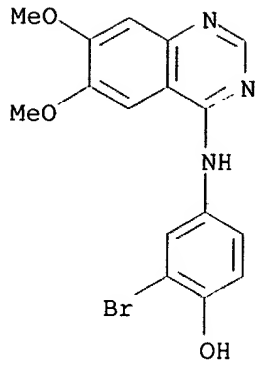


IT **211555-04-3P**, WHI-P154 **211555-08-7P**, WHI-P180

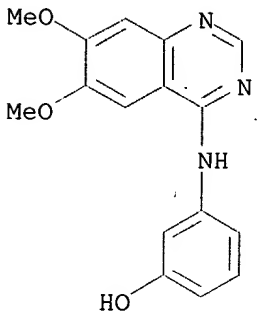
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

RN 211555-04-3 USPATFULL

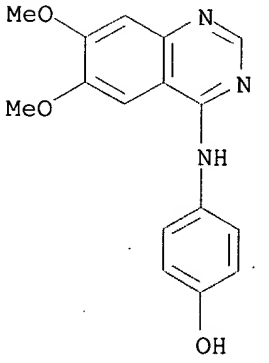
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-08-7 USPATFULL
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **202475-60-3P**, WHI-P131
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 202475-60-3 USPATFULL
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L81 ANSWER 5 OF 19 USPATFULL
ACCESSION NUMBER: 2003:106807 USPATFULL
TITLE: Chiral salt resolution
INVENTOR(S): Wilcox, Glenn E., UNITED STATES
Flanagan, Mark E., UNITED STATES
Munchhof, Michael J., UNITED STATES
Vries, Ton, UNITED STATES

Koecher, Christian, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003073719	A1	20030417
APPLICATION INFO.:	US 2002-154699	A1	20020523 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-294775P	20010531 (60)
	US 2001-341048P	20011206 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
LINE COUNT: 1666
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for resolving enantiomers of a compound containing the structure of the formula: ##STR1##

wherein R.sup.4or R.sup.5 may contain one or more asymmetric centers, by mixing a racemic mixture of enantiomers of a compound, containing the structure of said formula; in a solvent, with a resolving compound having a defined stereospecificity, to form a solution and with said resolving agent being capable of binding with at least one but not all of said enantiomers to form a precipitate, containing said at least one of said enantiomers in stereospecific form and collecting either the precipitate and purifying it or collecting the solution with contained other of said enantiomers and recrystallizing the enantiomer contained in said solution.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **157482-36-5, Janus Kinase 3**
(**inhibitors;** optical resoln. of (1-benzyl-4-methylpiperidin-3-yl)-methylamine and the use thereof for prepn. of pyrrolo[2,3-d]pyrimidines as protein kinase inhibitors)
RN 157482-36-5 USPATFULL
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

STRUCTURE DIAGRAM IS NOT AVAILABLE

L81 ANSWER 6 OF 19 USPATFULL
ACCESSION NUMBER: 2002:78855 USPATFULL
TITLE: Therapeutic compounds
INVENTOR(S): Uckun, Fatih M., White Bear Lake, MN, UNITED STATES
Sudbeck, Elise A., St. Paul, MN, UNITED STATES
Cetkovic, Marina, Maplewood, MN, UNITED STATES
Malaviya, Ravi, Shoreview, MN, UNITED STATES
Liu, Xing-Ping, Minneapolis, MN, UNITED STATES
PATENT ASSIGNEE(S): Parker Hughes Institute, St. Paul, MN (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002042513	A1	20020411
	US 6469013	B2	20021022
APPLICATION INFO.:	US 2001-858824	A1	20010516 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-688756, filed on 16 Oct 2000, PENDING Division of Ser. No. US 1999-378093, filed on 20 Aug 1999, GRANTED, Pat. No. US 6313129

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-97365P	19980821 (60)
	US 1998-97359P	19980821 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Denise M Kettelberger Ph D, P O BOX 2903, Minneapolis, MN, 55402-0903	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	55 Drawing Page(s)	
LINE COUNT:	2453	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

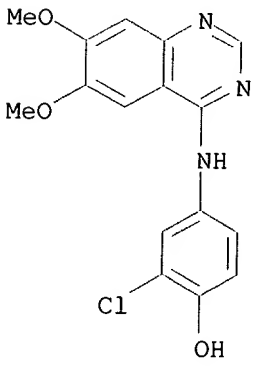
AB The invention provides novel **JAK-3 inhibitors** that are useful for treating leukemia and lymphoma. The compounds are also useful to treat or prevent **skin cancer**, as well as **sunburn** and **UVB**-induced skin **inflammation**. In addition, the compounds of the present invention prevent the immunosuppressive effects of **UVB** radiation, and are useful to treat or prevent autoimmune diseases, **inflammation**, and transplant rejection. The invention also provides pharmaceutical compositions comprising compounds of the invention, as well as therapeutic methods for their use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **211555-09-8P**, WHI-P 197
(WHI-P 197; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

RN 211555-09-8 USPATFULL

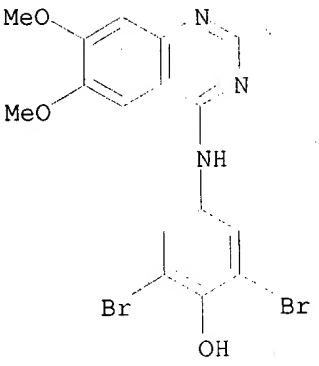
CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



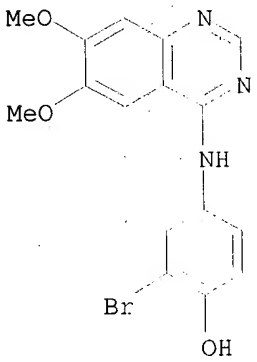
IT **211555-05-4P**, WHI-P 97
(WHI-P 97; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

RN 211555-05-4 USPATFULL

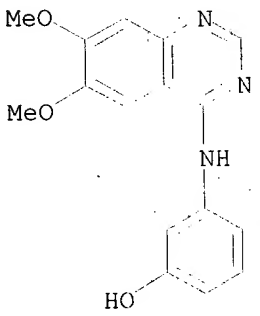
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



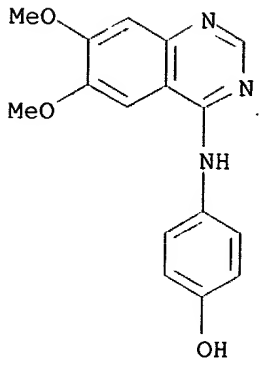
IT **211555-04-3P**, WHI-P154 **211555-08-7P**, WHI-P180
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 211555-04-3 USPATFULL
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-08-7 USPATFULL
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **202475-60-3P**, WHI-P131
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 202475-60-3 USPATFULL
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L81 ANSWER 7 OF 19 USPATFULL

ACCESSION NUMBER: 2001:212446 USPATFULL
TITLE: Dimethoxy quinazolines for treating diabetes
INVENTOR(S): Uckun, Fatih M., White Bear Lake, MN, United States
Sudbeck, Elise A., St. Paul, MN, United States
Cetkovic, Marina, Maplewood, MN, United States
Malaviya, Ravi, Shoreview, MN, United States
Liu, Xing-Ping, Minneapolis, MN, United States
PATENT ASSIGNEE(S): Parker Hughes Institute, Roseville, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001044442	A1	20011122
	US 6495556	B2	20021217
APPLICATION INFO.:	US 2001-812098	A1	20010319 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-378093, filed on 20 Aug 1999, PENDING

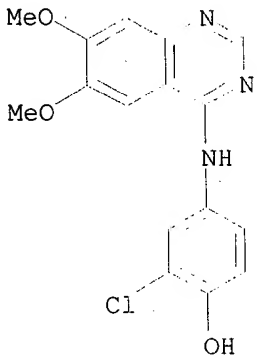
	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-97365P	19980821 (60)
	US 1998-97359P	19980821 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 55 Drawing Page(s)
LINE COUNT: 2449
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

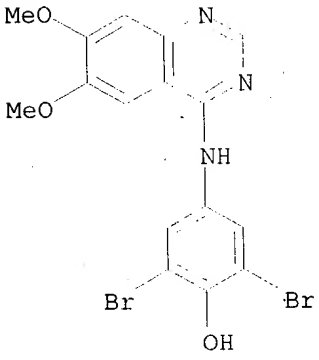
AB The invention provides novel **JAK-3 inhibitors** that are useful for treating leukemia and lymphoma. The compounds are also useful to treat or prevent **skin cancer**, as well as **sunburn** and **UVB**-induced skin **inflammation**. In addition, the compounds of the present invention prevent the immunosuppressive effects of **UVB** radiation, and are useful to treat or prevent autoimmune diseases, **inflammation**, and transplant rejection. The invention also provides pharmaceutical compositions comprising compounds of the invention, as well as therapeutic methods for their use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **211555-09-8P**, WHI-P 197
(WHI-P 197; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)

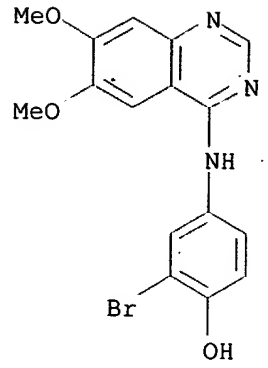
RN 211555-09-8 USPATFULL
CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



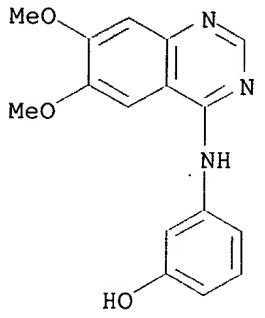
IT **211555-05-4P**, WHI-P 97
(WHI-P 97; therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 211555-05-4 USPATFULL
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



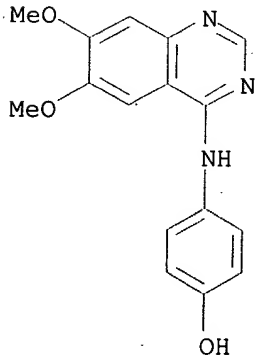
IT **211555-04-3P**, WHI-P154 **211555-08-7P**, WHI-P180
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 211555-04-3 USPATFULL
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-08-7 USPATFULL
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **202475-60-3P**, WHI-P131
(therapeutic uses of quinazoline derivs. as **JAK-3** kinase **inhibitors**)
RN 202475-60-3 USPATFULL
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L81 ANSWER 8 OF 19 USPATFULL
ACCESSION NUMBER: 1998:7076 USPATFULL
TITLE: Aryl and heteroaryl quinazoline compounds which inhibit EGF and/or PDGF receptor tyrosine kinase
INVENTOR(S): Myers, Michael R., Reading, PA, United States
Spada, Alfred P., Lansdale, PA, United States
Maguire, Martin P., Mont Clare, PA, United States

PATENT ASSIGNEE(S): Persons, Paul E., King of Prussia, PA, United States
Rhone-Poulenc Rorer Pharmaceuticals Inc., Collegeville, PA, United States (U.S. corporation)

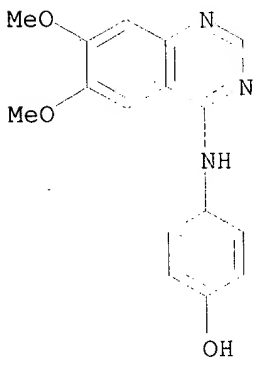
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5710158		19980120
APPLICATION INFO.:	US 1994-229886		19940419 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-166199, filed on 23 Dec 1993, now patented, Pat. No. US 5480883 which is a continuation-in-part of Ser. No. US 1992-988515, filed on 10 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-698420, filed on 10 May 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose G.
ASSISTANT EXAMINER: Cebulak, Mary C.
LEGAL REPRESENTATIVE: Parker, III, Raymond S., Nicholson, James A., Savitzky, Martin F.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 1107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the modulation and/or inhibition of cell signaling, cell proliferation, cell **inflammatory** response, the control of abnormal cell growth and cell reproduction. More specifically, this invention relates to the use of mono- and/or bicyclic aryl or heteroaryl quinazoline compounds in inhibiting cell proliferation, including compounds which are useful protein tyrosine kinase (PTK) inhibitors. The method of treating cell proliferation using said quinazoline compounds and their use in pharmaceutical compositions is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **202475-60-3**
(aryl and heteroaryl quinazoline compds. which inhibit EGF and/or PDGF receptor tyrosine kinase)
RN 202475-60-3 USPATFULL
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L81 ANSWER 9 OF 19 MEDLINE
ACCESSION NUMBER: 2001273665 MEDLINE

DOCUMENT NUMBER: 21260736 PubMed ID: 11368440
TITLE: Constitutive STAT3-activation in Sezary syndrome: tyrphostin AG490 inhibits STAT3-activation, interleukin-2 receptor expression and growth of leukemic Sezary cells.
AUTHOR: Eriksen K W; Kaltoft K; Mikkelsen G; Nielsen M; Zhang Q; Geisler C; Nissen M H; Ropke C; Wasik M A; Odum N
CORPORATE SOURCE: Institute of Medical Microbiology and Immunology, University of Copenhagen, Denmark.
CONTRACT NUMBER: CA89194 (NCI)
SOURCE: LEUKEMIA, (2001 May) 15 (5) 787-93.
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531

ABSTRACT:
Interleukin-2 (IL-2) is a growth factor which upon binding to high-affinity receptors (IL-2Ralphabetagamma) triggers mitogenesis in T cells. IL-2Ralpha expression is restricted to T cells which have recently encountered antigen, and in healthy individuals the majority (>95%) of peripheral T cells are IL-2Ralpha negative. An aberrant expression of IL-2Ralpha has recently been described in cutaneous T-cell lymphoma (CTCL). Here, we study the regulation of IL-2Ralpha expression and STATs in a tumor cell line obtained from peripheral blood from a patient with Sezary syndrome (SS), a leukemic variant of CTCL. We show that (1) STAT3 (a transcription factor known to regulate IL-2Ralpha transcription) is constitutively tyrosine-phosphorylated in SS tumor cells, but not in non-malignant T cells; (2) STAT3 binds constitutively to a STAT-binding sequence in the promotor of the IL-2Ralpha gene; (3) the Janus kinase inhibitor, tyrphostine AG490, inhibits STAT3 activation, STAT3 DNA binding, and IL-2Ralpha mRNA and protein expression in parallel; and (4) tyrphostine AG490 inhibits IL-2 driven mitogenesis and triggers apoptosis in SS tumor cells. In conclusion, we provide the first example of a constitutive STAT3 activation in SS tumor cells. Moreover, our findings suggest that STAT3 activation might play an important role in the constitutive IL-2Ralpha expression, survival, and growth of malignant SS cells.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antineoplastic Agents: PD, pharmacology
Apoptosis: DE, drug effects
*DNA-Binding Proteins: ME, metabolism
Phosphorylation
***Protein-Tyrosine Kinase: AI, antagonists & inhibitors**
Protein-Tyrosine Kinase: ME, metabolism
Receptors, Interleukin-2: AN, analysis
Sezary Syndrome: DT, drug therapy
*Sezary Syndrome: ME, metabolism
Sezary Syndrome: PA, pathology
Skin Neoplasms: DT, drug therapy
***Skin Neoplasms: ME, metabolism**
Skin Neoplasms: PA, pathology
*Trans-Activators: ME, metabolism
Tumor Cells, Cultured
*Tyrphostins: PD, pharmacology
CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (DNA-Binding Proteins); 0 (Receptors, Interleukin-2); 0 (Stat3 protein); 0 (Trans-Activators); 0 (Tyrphostins); 0 (tyrphostin AG-490); EC 2.7.1.- (**Janus kinase 3**); EC 2.7.1.112 (Protein-Tyrosine Kinase)

L81 ANSWER 10 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003083034 EMBASE
TITLE: The suppressor of cytokine signaling-1 (SOCS1) is a novel therapeutic target for enterovirus-induced cardiac injury.
AUTHOR: Yasukawa H.; Yajima T.; Duplain H.; Iwatate M.; Kido M.; Hoshijima M.; Weitzman M.D.; Nakamura T.; Woodard S.; Xiong D.; Yoshimura A.; Chien K.R.; Knowlton K.U.
CORPORATE SOURCE: K.U. Knowlton, Department of Medicine, Institute of Molecular Medicine, University of California, 9500 Gilman Drive, San Diego, CA 92093-0613K, United States. kknowlton@ucsd.edu
SOURCE: Journal of Clinical Investigation, (2003) 111/4 (469-478). Refs: 47
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Enteroviral infections of the heart are among the most commonly identified causes of acute myocarditis in children and adults and have been implicated in dilated cardiomyopathy. Although there is considerable information regarding the cellular immune response in myocarditis, little is known about innate signaling mechanisms within the infected cardiac myocyte that contribute to the host defense against viral infection. Here we show the essential role of Janus kinase (JAK) signaling in cardiac myocyte antiviral defense and a negative role of an intrinsic JAK inhibitor, the suppressor of cytokine signaling (SOCS), in the early disease process. Cardiac myocyte-specific transgenic expression of SOCS1 inhibited enterovirus-induced signaling of JAK and the signal transducers and activators of transcription (STAT), with accompanying increases in viral replication, cardiomyopathy, and mortality in coxsackievirus-infected mice. Furthermore, the inhibition of SOCS in the cardiac myocyte through adeno-associated virus-mediated (AAV-mediated) expression of a dominant-negative SOCS1 increased the myocyte resistance to the acute cardiac injury caused by enteroviral infection. These results indicate that strategies directed at inhibition of SOCS in the heart and perhaps other organs can augment the host-cell antiviral system, thus preventing viral-mediated endorgan damage during the early stages of infection.

CONTROLLED TERM: Medical Descriptors:
*heart injury: ET, etiology
*Enterovirus
myocarditis: ET, etiology
heart dilatation: ET, etiology
cellular immunity
signal transduction
host resistance
virus infection
nonhuman
mouse
animal experiment
animal model
controlled study
animal cell
article
priority journal
Drug Descriptors:
*cytokine: EC, endogenous compound
*suppressor of cytokine signaling 1

***enzyme inhibitor**
Janus kinase
unclassified drug
CAS REGISTRY NO.: (Janus kinase) 161384-16-3

L81 ANSWER 11 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002445353 EMBASE
TITLE: The phosphotidyl inositol 3-kinase/Akt signal pathway is involved in interleukin-6-mediated Mcl-1 upregulation and anti-apoptosis activity in basal cell carcinoma cells.
AUTHOR: Jee S.H.; Chiu H.C.; Tsai T.F.; Tsai W.L.; Liao Y.H.; Chu C.Y.; Kuo M.-L.
CORPORATE SOURCE: Dr. M.-L. Kuo, Laboratory of Molecular Toxicology, Institute of Toxicology, No. 1, Sec., 1, Jen-Ai Road, Taipei, Taiwan,Province of China. toxkml@ha.mc.ntu.edu.tw
SOURCE: Journal of Investigative Dermatology, (2002) 119/5 (1121-1127).
Refs: 52
ISSN: 0022-202X CODEN: JIDEAE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Dysregulation of interleukin-6 has been reported to be associated with various types of tumors, and interleukin-6 plays an important part in regulating apoptosis in many types of cells. Previously, Mcl-1 was shown to be significantly increased in interleukin-6-overexpressed basal cell carcinoma cells and conferred on them anti-apoptotic activity. The aim of this study was to investigate which signaling pathway is involved in the anti-apoptotic effect of interleukin-6 on basal cell carcinoma cells. Here we show that the addition of recombinant 100 ng per ml interleukin-6 to basal cell carcinoma cells induced a 2.3-fold increase in the level of Mcl-1 protein in basal cell carcinoma cells. Transfection with dominant-negative STAT3 (STAT3F) into interleukin-6-treated basal cell carcinoma cells caused a decrease of phosphotyrosyl STAT3 but did not alter Mcl-1 protein levels; however, AG490, a Janus tyrosine kinase inhibitor, was capable of inhibiting the interleukin-6-induced elevation of Mcl-1 protein. Next, interleukin-6 stimulation elicited extracellular signal-regulated kinase activation in basal cell carcinoma cells, and the mitogen-activated protein kinase inhibitor, PD98059, could affect this response without affecting the interleukin-6-mediated Mcl-1 upregulation. Use of the two phosphotidyl inositol 3-kinase inhibitors, LY294002 and wortmannin, to check whether this pathway is involved in Mcl-1 upregulation by interleukin-6, we found that the phosphotidyl inositol 3-kinase inhibitors completely attenuated the interleukin-6-induced Mcl-1 upregulation. Furthermore, in the interleukin-6-overexpressing basal cell carcinoma cell clone, dominant-negative Akt also significantly reduced the increased level of Mcl-1. Interestingly, Janus tyrosine kinase inhibitor, AG490, treatment strongly blocked the phosphotidyl inositol 3-kinase pathway activation, as evidenced by the decrease in phospho-Akt level. Blockage of phosphotidyl inositol 3-kinase/Akt pathway abolished the interleukin-6-mediated anti-apoptotic activity in ultraviolet B treated cells. Unexpectedly, without ultraviolet B irradiation, STAT3F transfection also induced a significant apoptosis in basal cell carcinoma/interleukin-6 cells. Taken together, our data suggest that both the phosphotidyl inositol 3-kinase/Akt and STAT3 pathways are potentially involved in interleukin-6-mediated cell survival activity in basal cell carcinoma cells; however, the upregulation of the anti-apoptotic Mcl-1 protein by interleukin-6 is mainly through the Janus tyrosine kinase/phosphotidyl inositol 3-kinase/Akt, but not the STAT3 pathway.

CONTROLLED TERM: Medical Descriptors:
*signal transduction
***basal cell carcinoma**
***skin carcinoma**
upregulation
apoptosis
carcinoma cell
cell level
genetic transfection
amino acid sequence
enzyme activation
drug effect
cell clone
protein expression
protein function
ultraviolet B radiation
cell survival
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*phosphatidylinositol 3 kinase
*protein kinase B
*protein mcl 1: EC, endogenous compound
interleukin 6
STAT3 protein
meta tyrosine
n benzyl 2 cyano 3 (3,4 dihydroxyphenyl)acrylamide: PD, pharmacology
Janus kinase
enzyme inhibitor: PD, pharmacology
mitogen activated protein kinase inhibitor: PD, pharmacology
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
2 morpholino 8 phenylchromone: PD, pharmacology
phosphatidylinositol 3 kinase inhibitor: PD, pharmacology
wortmannin: PD, pharmacology

CAS REGISTRY NO.: (phosphatidylinositol 3 kinase) 115926-52-8; (protein kinase B) 148640-14-6; (meta tyrosine) 2180-37-2, 775-06-4; (n benzyl 2 cyano 3 (3,4 dihydroxyphenyl)acrylamide) 133550-30-8; (Janus kinase) 161384-16-3; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (2 morpholino 8 phenylchromone) 154447-36-6; (wortmannin) 19545-26-7

CHEMICAL NAME: (1) Ag 490; (2) Pd 98059; (3) Ly 294002

COMPANY NAME: (3) Calbiochem (United States)

L81 ANSWER 12 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002445349 EMBASE

TITLE: Cyclooxygenase-2 inhibitor enhances whereas prostaglandin E(2) inhibits the production of interferon-induced protein of 10 kDa in epidermoid carcinoma A431.

AUTHOR: Kanda N.; Watanabe S.

CORPORATE SOURCE: N. Kanda, Department of Dermatology, Teikyo University, School of Medicine, 11-1, Kaga-2, Itabashi-ku, Tokyo 173-8605, Japan. nmk@med.teikyo-u.ac.jp

SOURCE: Journal of Investigative Dermatology, (2002) 119/5 (1080-1089).
Refs: 51
ISSN: 0022-202X CODEN: JIDEAE

COUNTRY: United States

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Interferon-induced protein of 10 kDa (IP-10) induces antitumor immunity. Cyclooxygenase-2 and its metabolite prostaglandin E2 (PGE(2)) are overexpressed in tumor cells, which may suppress antitumor immunity. We examined the in vitro effects of cyclooxygenase-2 inhibitor NS398 on IP-10 production in human epidermoid carcinoma A431. NS398 enhanced interferon-.gamma.-induced IP-10 secretion, mRNA expression, and promoter activation in A431, and exogenous PGE(2) antagonized the enhancement. Interferon-stimulated response element (ISRE) on IP-10 promoter was responsible for the transcriptional regulation by NS398 and PGE(2). NS398 enhanced interferon-.gamma.-induced transcription through ISRE and binding of signal transducer and activator of transcription 1.alpha. (STAT1.alpha. to ISRE in A431, and PGE(2) antagonized the enhancement. NS398 enhanced interferon-.gamma.-induced tyrosine phosphorylation of STAT1.alpha., Janus tyrosine kinase 1, and Janus tyrosine kinase 2, and PGE(2) antagonized the enhancement. PGE(2)-mediated suppression of IP-10 synthesis was counteracted by adenylate cyclase inhibitor SQ22536 and protein kinase A inhibitor H-89, and PGE(2) receptor EP4 antagonist AH23848B. AH23848B, SQ22536, and H-89 counteracted the PGE(2)-mediated suppression of ISRE-dependent transcription, STAT1.alpha. binding to ISRE, and tyrosine phosphorylation of STAT1.alpha., Janus tyrosine kinase 1, and Janus tyrosine kinase 2. PGE(2) increased intracellular cAMP level and protein kinase A activity in A431 pretreated with NS398, and AH23848B blocked the effects of PGE(2). These results suggest that A431-derived PGE(2) may generate cAMP signal via EP4 in A431, which may activate protein kinase A, and may resultantly inhibit interferon-.gamma.-induced STAT1.alpha. activation and IP-10 synthesis. The results also suggest that NS398 may restore IP-10 synthesis by preventing PGE(2) production in A431 and thus may be therapeutically useful for skin cancer.

CONTROLLED TERM:
Medical Descriptors:
*squamous cell carcinoma
***skin carcinoma**
molecular weight
in vitro study
drug effect
protein secretion
protein expression
drug antagonism
transcription regulation
protein binding
protein phosphorylation
protein synthesis
cell level
enzyme activity
signal transduction
human
controlled study
human cell
article
priority journal
Drug Descriptors:
***prostaglandin E2**
*n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide: PD, pharmacology
gamma interferon
protein

cyclooxygenase 2 inhibitor: PD, pharmacology
messenger RNA
STAT1 protein
protein subunit
Janus kinase
adenylate cyclase
enzyme inhibitor: PD, pharmacology
9 (tetrahydro 2 furyl)adenine: PD, pharmacology
cyclic AMP dependent protein kinase inhibitor: PD, pharmacology
n [2 (4 bromocinnamylamino)ethyl] 5 isoquinolinesulfonamide: PD, pharmacology
prostaglandin receptor blocking agent: PD, pharmacology
7 [5 (4 biphenylylmethoxy) 2 morpholino 3 oxocyclopentyl] 4 heptenoic acid: PD, pharmacology
cyclic AMP: EC, endogenous compound
receptor subtype
5 (4 chlorophenyl) 1 (4 methoxyphenyl) 3 trifluoromethyl 1h pyrazole: PD, pharmacology

CAS REGISTRY NO.: (prostaglandin E2) 363-24-6; (n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide) 123653-11-2; (gamma interferon) 82115-62-6; (protein) 67254-75-5; (Janus kinase) 161384-16-3; (adenylate cyclase) 9012-42-4; (9 (tetrahydro 2 furyl)adenine) 17318-31-9; (n [2 (4 bromocinnamylamino)ethyl] 5 isoquinolinesulfonamide) 127243-85-0; (7 [5 (4 biphenylylmethoxy) 2 morpholino 3 oxocyclopentyl] 4 heptenoic acid) 81443-73-4; (cyclic AMP) 60-92-4; (5 (4 chlorophenyl) 1 (4 methoxyphenyl) 3 trifluoromethyl 1h pyrazole) 188817-13-2

CHEMICAL NAME: (1) Ns 398; (2) Sq 22536; (3) H 89; (4) Ah 23848b; (5) Sc 560

COMPANY NAME: (4) Funakoshi (Japan); (5) Calbiochem (United States)

L81 ANSWER 13 OF 19 DRUGU COPYRIGHT 2003 THOMSON DERWENTDUPLICATE 3
ACCESSION NUMBER: 2001-16277 DRUGU B P
TITLE: Oncostatin M-induced matrix metalloproteinase and tissue inhibitor of metalloprteinase-3 genes expression in chondrocytes requires janus kinase/STAT signaling pathway.
AUTHOR: Li W Q; Dehnade F; Zafarullah M
CORPORATE SOURCE: Univ.Montreal
LOCATION: Montreal, Que., Can.
SOURCE: J.Immunol. (166, No. 5, 3491-98, 2001) 8 Fig. 68 Ref.
CODEN: JOIMA3 ISSN: 0022-1767
AVAIL. OF DOC.: K-5255 Mailloux, Hopital Notre-Dame du Centre Hospitalier de l; Universite de Montreal, 15600 Sherbrooke est, Montreal, Quebec, Canada H2L 4M1. (Email: Muhammad.Zafarullah@umontreal.ca).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

In the present study the Authors investigated signaling pathways regulating the induction of MMP and TIMP-3 genes by OSM. OSM induced MMP and TIMP-3 genes in chrondrocytes by activating JAK/STAT and mitogen-activated protein kinase signaling cascades, and interference with these pathways may be a useful approach to block the catabolic actions of OSM. The catabolic responses of OSM such as promotion of cartilage degradation in arthritis could possibly be blocked by the inhibitors of JAK.STAT and MAPK signaling cascades such as ***JAK3*** **inhibitor** and curcumin.

SECTION HEADING: B Biochemistry
P Pharmacology

CLASSIF. CODE: 14 Enzyme Inhibitors
20 Immunological
24 Bones and Joints
27 Molecular Biology

CONTROLLED TERM:
ONCOSTATIN-M *RC; MATRIX-METALLOPROTEINASE *FT; METALLOPROTEINASE *FT; GENE *FT; EXPRESSION *FT; MODE-OF-ACT. *FT; DNA *FT; BINDING *FT; RNA *FT; IN-VITRO *FT; CHONDROCYTE *FT; GENETICS *FT; CARTILAGE *FT
[01] AG-490 *PH; AG-490 *RN; TRIAL-PREP. *FT; PH *FT
[02] CURCUMIN *PH; CURCUMIN *RN; **ANTIINFLAMMATORIES** *FT; PHOSPHOLIPASE-INHIBITORS *FT; PH *FT
CAS REGISTRY NO.: 458-37-7
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L81 ANSWER 14 OF 19 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-14402 DRUGU P
TITLE: **Inhibition** of **JAK3** and STAT6 tyrosine phosphorylation by the immunosuppressive drug leflunomide leads to a block in IgG1 production.
AUTHOR: Siemasko K; Chong A S F; Jack H M; Gong H; Williams J W; Finnegan A
CORPORATE SOURCE: Univ.Loyola
LOCATION: Chicago, Ill., USA
SOURCE: J.Immunol. (160, No. 4, 1581-88, 1998) 7 Fig. 1 Tab. 45 Ref.
CODEN: JOIMA3 ISSN: 0022-1767
AVAIL. OF DOC.: Section of Rheumatology, Rush-Presbyterian-St. Luke's Medical Center, 1653 W. Congress Parkway, Chicago, IL 60612, U.S.A. (A.F.).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The hypothesis that leflunomide (LF) prevents Ig production through inhibition of tyrosine kinase (TK) activity was investigated in-vitro in mice B cells. LF appeared to act as a pyrimidine synthesis inhibitor to suppress B cell proliferation and IgM secretion. LF blocked IgG1 secretion and IL-4 induced TK activity independent of its effects on B cell proliferation. LF suppressed IL-4 induced tyrosine phosphorylation of JAK3 and STAT6 and prevented STAT6 binding to the STAT6 DNA binding site found in the IgG1 promoter. The results suggest that LF blocks IgG1 production through its ability to prevent tyrosine phosphorylation of intracellular proteins required for IgG1 production.

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 20 Immunological
50 Biological Response Modifiers

CONTROLLED TERM:
[01] LEFLUNOMIDE *PH; LEFLUNOMI *RN; IMMUNOSUPPRESSIVE *FT; IN-VITRO *FT; MODE-OF-ACT. *FT; MOUSE *FT; B-CELL *FT; IGM *FT; IGG *FT; SECRETION *FT; PROLIFERATION *FT; TYROSINE *FT; PHOSPHORYLATION *FT; LAB.ANIMAL *FT; LYMPHOCYTE *FT; IMMUNOGLOBULIN *FT; IMMUNOGLOBULIN *FT; ANTIRHEUMATICS *FT; IMMUNOSUPPRESSIVES *FT; **ANTIINFLAMMATORIES** *FT; PH *FT
CAS REGISTRY NO.: 75706-12-6
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L81 ANSWER 15 OF 19 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-43115 DRUGU P
TITLE: Interference in IL-2 receptor mediated signal transduction by the hydroxylamine metabolite of sulfamethoxazole.
AUTHOR: Hess D A; Lee J; Madrenas Q; Rieder M J
CORPORATE SOURCE: Univ.Western-Ontario
LOCATION: London, Ont., Can.
SOURCE: J.Clin.Pharmacol. (38, No. 9, 846, 1998)
CODEN: JCPCBR ISSN: 0091-2700
AVAIL. OF DOC.: Department of Paediatrics, Children's Hospital of Western Ontario, London, Ontario, Canada.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Sulfamethoxazole hydroxylamine (SMX-HA) drastically reduced supernatant levels of IL-1beta, TNF-alpha and IL-4 protein in peripheral blood mononuclear cells (PBMC) in-vitro. At 25 uM, SMX-HA reduced IL-1beta, TNF-alpha and IL-4 production to 7.8%, 22.1% and 24.6% respectively. SMX-HA 25 uM did not affect IL-2 production. Immunoblot analysis of IL-2 receptor (IL-2R) mediated Janus kinase activation revealed diminished phosphorylation of Jak1 and Jak3 in SMX-HA treated, PHA/recombinant IL-2 activated PBMC. SMX-HA did not ***inhibit*** **Jak3** association with the IL-2R gamma chain. The results suggest that SMX-HA interferes with IL-2R mediated signal transduction resulting in reduced production of **inflammatory** cytokines and overall inhibition of T lymphocyte proliferation. (conference abstract). (No EX).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 20 Immunological
50 Biological Response Modifiers

CONTROLLED TERM:
[01] SULFAMETHOXAZOLE-HYDROXYLAMINE *PH; DR9502277 *RN; PERIPHERAL *FT; MONOCYTE *FT; IN-VITRO *FT; IMMUNOSUPPRESSIVE *FT; MODE-OF-ACT. *FT; INTERLEUKIN-2-RECEPTOR *FT; INTERLEUKIN-1-BETA *FT; INTERLEUKIN-2 *FT; INTERLEUKIN-4 *FT; TUMOR-NECROSIS-FACTOR-ALPHA *FT; BIOSYNTH. *FT; LEUKOCYTE *FT; INTERLEUKIN-RECEPTOR *FT; RECEPTOR *FT; IMMUNOSUPPRESSIVES *FT; SYNERGISTS *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L81 ANSWER 16 OF 19 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2002:35078220 BIOTECHNO
TITLE: Human lung myofibroblasts as effectors of the **inflammatory** process: The common receptor .gamma. chain is induced by Th2 cytokines, and CD40 ligand is induced by lipopolysaccharide, thrombin and TNF-.alpha.
AUTHOR: Doucet C.; Giron-Michel J.; Canonica G.W.; Azzarone B.
CORPORATE SOURCE: B. Azzarone, U506 INSERM, Hopital P. Brousse, 16 Av. P.V. Couturier, F-94807 Villejuif, France.
E-mail: bazzarone@hotmail.com
SOURCE: European Journal of Immunology, (2002), 32/9 (2437-2449), 43 reference(s)
CODEN: EJIMAF ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English

Searched by Barb O'Bryen, STIC 308-4291

ABSTRACT: The common .gamma. (.gamma.c) chain, shared by Th1 and Th2 cytokines, is fundamental for the activation of hematopoietic cells, but its role in non-hematopoietic tissues has not been explored. Here we show that in normal lung fibroblasts IL-4 and IL-13 induce the expression of the .gamma.c chain and its association with Janus kinase (JAK) 3, while lung myofibroblasts constitutively express a .gamma.c chain displaying a limited association with JAK3. In the latter cells, without exogenous cytokines, .gamma.c/JAK3 controls, through autocrine loops, tyrosine kinase (TYK) 2 phosphorylation and the balance between functional (IL-4R.alpha., IL-13R.alpha.1) and decoy (IL-13R.alpha.2) high-affinity receptors. Moreover, JAK3 is also associated with a prephosphorylated IL-4R.alpha. and CD40. This novel "heterotrimer" (p-IL-4R.alpha., CD40/JAK3) is functional and controls STAT3 phosphorylation and CD40 expression, as shown by use of the specific **JAK3 inhibitor** WHI-P31. In basal culture conditions, CD40 signaling could be induced by the transient establishment of inter-fibroblastic CD40/CD40 ligand (CD40L) functional bridges. Indeed, powerful pro-**inflammatory** stimuli such as lipopolysaccharide and thrombin can rapidly mobilize CD40L at the surface of lung myofibroblasts. These interactions are modified by IL-13, which triggers the formation of a new type of functional receptor (p-IL-4R.alpha./IL-13R.alpha.1/.gamma.c) and also the recruitment and the phosphorylation of **JAK3**. Treatment with **JAK3 inhibitors** blocks IL-13-induced phosphorylation of JAK2, TYK2 and STAT3, but not of JAK1 and STAT6. These data underline (1) the pivotal role of the .gamma.c chain, CD40/CD40L, JAK3 and IL-13 in the **inflammatory**-like activation of lung myofibroblasts, (2) the cell-type restraint effects of IL-13 on these cells, and (3) the potential usefulness of **JAK3 inhibitors** in the treatment of asthma.

CONTROLLED TERM: *interleukin 4 receptor; *cytokine; *CD40 ligand; *lipopolysaccharide; *thrombin; *tumor necrosis factor alpha; lung fibroblast; effector cell; **inflammation**; Th2 cell; protein expression; myofibroblast; autocrine effect; enzyme phosphorylation; receptor affinity; protein phosphorylation; antigen expression; cell culture; signal transduction; cell surface; molecular interaction; cell activation; asthma; drug activity; human; controlled study; human cell; article; priority journal; interleukin 4; interleukin 13; Janus kinase; protein tyrosine kinase; interleukin 13 receptor; CD40 antigen; STAT3 protein; phosphotransferase inhibitor; STAT6 protein; whi p31

CAS REGISTRY NUMBER: (CD40 ligand) 226713-27-5; (thrombin) 9002-04-4; (interleukin 13) 148157-34-0; (Janus kinase) 161384-16-3; (protein tyrosine kinase) 80449-02-1

CHEMICAL NAME: Drug Trade Name: whi p31

L81 ANSWER 17 OF 19 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.

ACCESSION NUMBER: 1999:29301522 BIOTECHNO

TITLE: Genetic and biochemical evidence for a critical role of Janus kinase (JAK)-3 in mast cell-mediated type I hypersensitivity reactions

Searched by Barb O'Bryen, STIC 308-4291

AUTHOR: Malaviya R.; Uckun F.M.
CORPORATE SOURCE: F.M. Uckun, Hughes Institute, 2665 Long Lake Road, St. Paul, MN 55113, United States.
SOURCE: Biochemical and Biophysical Research Communications, (21 APR 1999), 257/3 (807-813), 25 reference(s)
CODEN: BBRCA0 ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: We investigated the role of JAK3 in IgE receptor/Fc.epsilon.RI-mediated mast cell responses. IgE/antigen induced degranulation and mediator release were substantially reduced with Jak3(-/-) mast cells from JAK3-null mice that were generated by targeted disruption of Jak3 gene in embryonic stem cells. Further, treatment of mast cells with 3'bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154), a potent **inhibitor** of **JAK3, inhibited** degranulation and proinflammatory mediator release after IgE receptor/Fc.epsilon.RI crosslinking. Thus, JAK3 plays a pivotal role in IgE receptor/Fc.epsilon.RI-mediated mast cell responses and targeting JAK3 may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions.
CONTROLLED TERM: *mitogen activated protein kinase; *mast cell; *immediate type hypersensitivity; immunoglobulin e receptor; Fc receptor; quinazoline derivative; protein kinase inhibitor; degranulation; stem cell; mediator release; **inflammation**; nonhuman; male; mouse; animal experiment; controlled study; animal cell; article; priority journal
CAS REGISTRY NUMBER: (mitogen activated protein kinase) 142243-02-5

L81 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2003:71032 BIOSIS
DOCUMENT NUMBER: PREV200300071032
TITLE: Dimethoxy quinazolines for treating diabetes.
AUTHOR(S): Uckun, Fatih M. (1); Sudbeck, Elise A.; Cetkovic, Marina; Malaviya, Ravi; Liu, Xing-Ping
CORPORATE SOURCE: (1) White Bear Leak, MN, USA USA
ASSIGNEE: Parker Hughes Institute
PATENT INFORMATION: US 6495556 December 17, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 17 2002) Vol. 1265, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ABSTRACT:
The invention provides novel **JAK-3 inhibitors** that are useful for treating leukemia and lymphoma. The compounds are also useful to treat or prevent **skin cancer**, as well as ***sunburn*** and **UVB**-induced skin **inflammation**. In addition, the compounds of the present invention prevent the immunosuppressive effects of **UVB** radiation, and are useful to treat or prevent autoimmune diseases, **inflammation**, and transplant rejection. The invention also provides pharmaceutical compositions comprising compounds of the invention, as well as therapeutic methods for their use.
NAT. PATENT. CLASSIF.:514266000

CONCEPT CODE: Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Metabolic Disorders *13020
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Endocrine System - Pancreas *17008
Integumentary System - Pathology *18506
Pharmacology - General *22002
Pharmacology - Endocrine System *22016
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

INDEX TERMS: Major Concepts
Pharmacology

INDEX TERMS: Diseases
UVB-induced skin **inflammation**: injury, integumentary system disease; autoimmune disease: immune system disease; diabetes: drug therapy, endocrine disease/pancreas, metabolic disease; leukemia: blood and lymphatic disease, neoplastic disease; lymphoma: blood and lymphatic disease, immune system disease, neoplastic disease; **skin cancer**: integumentary system disease, neoplastic disease; **sunburn**: injury, integumentary system disease

INDEX TERMS: Chemicals & Biochemicals
JAK-3 inhibitors: enzyme **inhibitor** - drug; dimethoxy quinazolines: antidiabetic - drug

INDEX TERMS: Alternate Indexing
Autoimmune Diseases (MeSH); Diabetes Mellitus (MeSH); Leukemia (MeSH); Lymphoma (MeSH); **Skin Neoplasms** (MeSH); **Sunburn** (MeSH)

L81 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:482894 BIOSIS
DOCUMENT NUMBER: PREV199900482894
TITLE: Targeting Janus kinase 3 in mast cells prevents immediate hypersensitivity reactions and anaphylaxis.
AUTHOR(S): Malaviya, Ravi; Zhu, DeMin; Dibirdik, Ilker; Uckun, Fatih M. (1)
CORPORATE SOURCE: (1) Hughes Inst., 2665 Long Lake Rd., Suite 330, Saint Paul, MN, 55113 USA
SOURCE: Journal of Biological Chemistry, (Sept. 17, 1999) Vol. 274, No. 38, pp. 27028-27038.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Janus kinase 3 (JAK3), a member of the Janus family protein-tyrosine kinases, is expressed in mast cells, and its enzymatic activity is enhanced by IgE receptor/FcepsilonRI cross-linking. Selective **inhibition** of ***JAK3*** in mast cells with 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline) (WHI-P131) blocked the phospholipase C activation, calcium mobilization, and activation of microtubule-associated protein kinase after lgE receptor/FcepsilonRI cross-linking. Treatment of IgE-sensitized rodent as well as human mast cells with WHI-P131 effectively inhibited the activation-associated morphological changes, degranulation, and proinflammatory mediator release after specific antigen challenge without affecting the functional integrity of the distal secretory machinery. In vivo administration of the **JAK3 inhibitor** WHI-P131 prevented mast cell

degranulation and development of cutaneous as well as systemic fatal anaphylaxis in mice at nontoxic dose levels. Thus, JAK3 plays a pivotal role in IgE receptor/FcepsilonRI-mediated mast cell responses, and targeting ***JAK3*** with a specific **inhibitor**, such as WHI-P131, may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions.

CONCEPT CODE: Enzymes - General and Comparative Studies; Coenzymes *10802
Biochemical Methods - General *10050
Immunology and Immunochemistry - General; Methods *34502
Biochemical Studies - General *10060

BIOSYSTEMATIC CODE: Hominidae 86215
Muridae 86375

INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis)

INDEX TERMS: Parts, Structures, & Systems of Organisms
mast cells: immune system

INDEX TERMS: Chemicals & Biochemicals
Janus kinase 3: targeting

INDEX TERMS: Miscellaneous Descriptors
allergy; anaphylaxis; immediate hypersensitivity reaction; **inflammation**; signal transduction

ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISM: Organism Name
human (Hominidae); RBL-2H3 cell line (Muridae)

ORGANISM: Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

REGISTRY NUMBER: 157482-36-5 (JANUS KINASE 3)

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